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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/728,711	11/30/2000	Y. Tom Tang	21272-048CIP2C	4871

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EXAMINER	
EINSMANN, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/728,711	TANG ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-26 and 109* is/are rejected.

7)☒ Claim(s) *2 and 3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☒ Interview Summary (PTO-413) Paper No(s). 10 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-9 and 22-26 and SEQ ID NO: 1 in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

2. The effective filing date for the instantly elected claims is the instant filing date. Each of the instantly elected claims recites SEQ ID NO: 1 which is first disclosed in this application in its entirety (see interview summary, paper number 10).

Claim Objections

3. Claims 2 and 3 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 2 and 3 are of broader scope than claim 1 from which they depend, thus they fail to further limit the subject matter of claim 1. For example, claim 1 (the independent claim) requires that the isolated polynucleotide comprise SEQ ID NO: 1 or a mature protein coding portion of SEQ ID NO: 1. However, claim 2 is broader because it requires that the isolated polynucleotide encode a polypeptide with biological activity and hybridize under stringent conditions to the polynucleotide of claim 1, and thus, the polynucleotide of claim 2 could be a shorter portion of SEQ ID NO: 1, or a nucleic acid that has nucleotide differences from SEQ ID NO: 1. Claim 2 encompasses a larger genus than claim 1.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is further indefinite over the recitation "under stringent hybridization conditions" because it is not clear how this phrase is intended to limit the claim. The specification sets forth guidance on page 15 that "stringent" conditions are "conditions that are commonly understood in the art as stringent," and include highly stringent and moderately stringent conditions. However, the it is unclear how this language limits the claims because it is not clear what conditions it is meant to exclude or particularly include. Every level of hybridization has some degree of stringency, whether it be high stringency or low stringency.

Claim 3 is indefinite over the recitation "greater than about 99%" because it is not clear if 99% is meant to be a lower limit in this claim or some number less than 99%. The use of the word "about" prior to the lower limitation makes applications intentions in setting the lower limit unclear.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claim, the new limitation of "99% sequence identity" in claim 3 appears to represent new matter. The response identifies at least page 28, line 23 to page 29, line 4 of the specification as providing basis for this added limitation. However, the cited section is discussing 99% amino acid sequence identity, not nucleic acid sequence identity. The specification throughout discusses different levels of polynucleotide sequence identity (see pages 3, 16, and 18, for example) but does not appear to particularly discuss 99% nucleotide sequence identity. Since no basis has been identified, the claim is rejected as incorporating new matter.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-9 and 22-26 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility.

The pending claims have been reviewed in light of the the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The instant claims are drawn to nucleic acids, vectors, and host cells that comprise instant SEQ ID NO: 1 or a mature coding portion of SEQ ID NO: 1. The rejected claims also include a nucleic acid encoding a polypeptide with biological activity, wherein said polynucleotide has greater than about 99% sequence identity with SEQ ID NO: 1 or a mature coding portion of SEQ ID NO: 1, or wherein said polynucleotide hybridizes to the polynucleotide of claim 1 under stringent hybridization conditions. The specification teaches that SEQ ID NO: 1 was isolated from skeletal muscle and mammary gland tissues (Table 1, p. 104), that SEQ ID NO: 1 has a smith-waterman score of 1715 against Accession Number AL136365 (Table 2, p. 105), has some

homology with a portion of a herpes virus glycoprotein (Table 3, p. 106), and has a predicted DM DNA binding domain (Table 4, p. 107). The specification does not specifically assert a utility based on these particular identities.

The specification asserts a wide variety of general utilities for the claimed invention. For example, the specification teaches that the claimed nucleic acid can be useful in research to express recombinant proteins for analysis (p. 40), as a tissue marker, or as a molecular weight marker (p. 40). Furthermore, the specification asserts that each of the disclosed nucleic acids or polypeptides that they encode can be used as a nutritional source or a food supplement (p. 41). The specification teaches that the claimed nucleic acid or the polynucleotide that it encodes can be used in drug screening (p. 62), receptor activity assays (p. 63), to identify polymorphisms (p. 68), as a probe (p. 95). However, none of these utilities are specific to the instant polynucleotide or encoded polypeptide. Each of them applies to the broad class of nucleic acids or encoded polypeptides. That is, any nucleic acid or encoded polypeptide could be used for these purposes.

The specification further suggests a list of possible biological functions and utilities for the instant polynucleotide and/or encoded polypeptide. For example, the specification teaches that the polynucleotide may encode a cytokine (p. 41), a polypeptide with stem cell growth factor activity (p. 43), a polypeptide with activin/inhibin activity (p. 55). The specification teaches that the polynucleotide of the instant invention may be useful in cancer diagnosis and/or therapy (p. 57, or as an anti-inflammatory (p. 64). The possible uses and biological functions cited here are only a few in the extensive list provided by applicant on pages 41-67 of the specification. However, none of these is a substantial or credible utility for the instantly claimed SEQ ID NO: 1 because the specification has provided no reason to believe that instant SEQ ID NO: 1 has or

encodes a polypeptide with any of these activities. The specification merely suggests that the disclosed polynucleotide and polypeptide "may" have these activities. Further experimentation would be required in order to reasonably confirm any of these utilities as being associated with instant SEQ ID NO: 1 or the polypeptide encoded by instant SEQ ID NO: 1. Thus, these possible utilities are not substantial with regard to the claimed invention.

Finally, the prior art does not provide a well established utility that is specific, substantial, and credible with respect to instant SEQ ID NO: 1. First, the specification suggests that instant SEQ ID NO: 1 or the encoded polypeptide has homology with both a protein having a DM DNA binding domain and a herpes virus glycoprotein. The activity of these two different proteins is widely variant, and it is impossible to know from applicant's specification which activity can be assigned to instant SEQ ID NO: 1 or the polypeptide encoded by instant SEQ ID NO: 1. Thus, based on the disclosure of the specification, it is impossible to assign a well established utility to the claimed invention.

Furthermore, with regard to the DM binding domain, it is not clear or well established in the prior art that the presence of this domain imparts a particular activity on a polypeptide, let alone a specific, substantial and credible utility. Raymond et al. (Nature 1998) first describe the DM binding domain, and teach that a number of proteins in sequence databases appear to have this domain, but that the "function of these genes is unknown," thus highlighting the fact that the presence of a DM binding domain is not sufficient to establish a will known utility for a protein or for the nucleic acid encoding the protein. In a later paper, Raymond et al. (Developmental Biology, 1999), teach that DM domains may play a role in sexual development in a wide range of phyla (ABSTRACT), particularly providing several lines of evidence for the specific DM

domain gene Dmrt1's role in vertebrate gonad formation and/or sex determination. Raymond et al. teach that the similarity in structure of the Dmrt1 gene to other sex-determining genes "on its own is not compelling, as it is highly unlikely that all DM domain genes are involved in sex determination (p. 215)." In order to conclude that the Dmrt1 gene functions in gonad formation and/or sex determination, Raymond et al. particularly cite the expression data which indicates that the murine Dmrt1 gene expression is limited to the genital ridge as soon as that structure is morphologically distinct, and later becomes restricted to the sex cords of the testes (p. 215). In contrast, the instant specification teaches that SEQ ID NO: 1 is expressed in both skeletal muscle tissue and mammary glands (Table 1, p. 104). Furthermore, Meng et al. (Development, 1999) teach that a gene encoding a protein with high similarity to a DM binding domain and suggest that this gene is involved in early somitogenesis in zebrafish (ABSTRACT). Based on these teachings in the prior art, it is not possible to assign a biological function to instant SEQ ID NO: 1 solely on the basis of the possible presence of a DM binding domain, and it is concluded the prior art does not provide a well established utility for instant SEQ ID NO: 1 or the encoded polypeptide.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Claims 1-9 and 22-26 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial, specific, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The previous utility rejection discusses in depth the scope of the instant claims and the asserted utilities for the instantly claimed polynucleotides. For each of the reasons provided in the utility rejection, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention, because the specification fails to provide a specific, credible, and substantial utility for the claimed invention.

Claim Rejections - 35 USC § 112

9. Claims 1-9 and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to nucleic acids, vectors, and host cells that comprise instant SEQ ID NO: 1 or a mature coding portion of SEQ ID NO: 1. The rejected claims also include a

nucleic acid encoding a polypeptide with biological activity, wherein said polynucleotide has greater than about 99% sequence identity with SEQ ID NO: 1 or a mature coding portion of SEQ ID NO: 1, or wherein said polynucleotide hybridizes to the polynucleotide of claim 1 under stringent hybridization conditions. The specification provides a single working example of SEQ ID NO: 1. The specification does not identify within SEQ ID NO: 1 any particular "mature coding portions," nor does the specification give any indication as to which portions of SEQ ID NO: 1 might make up the mature coding portion. Furthermore, with regard to claims 2 and 3, these claims encompass sequences that are different from SEQ ID NO: 1 in that they may have nucleotide changes, additions or deletions. The claims require that the nucleic acid retain "biological activity," but neither the specification nor the claims provide any guidance as to how instant SEQ ID NO: 1 can be modified and still retain the same biological function. The instant claims encompass variants and homologues of SEQ ID NO: 1, which may or may not function in the same was as SEQ ID NO: 1, provided that they maintain some biological activity. Biological activity could include the ability to act as a substrate for a protease. However, none of these sequences that differ from SEQ ID NO: 1 meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed* (See page 1117)." The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed (See Vas-Cath at page 1116)."

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> It is noted that in Fiers v. Revel (25 USPQ2d, 1601), the Fed. Cir. concluded that
>
> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only nucleic acids consisting of instant SEQ ID NO: 1 is described.

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of nucleic acids which are a "mature coding portion" of SEQ ID NO: 1, or which have nucleotides modified by any addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 1 yet remain any particular biological activity. Therefore, only nucleic acids comprising instant SEQ ID NO: 1 but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph.

The species specifically disclosed are not representative of the genus because the genus is highly variant.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 2 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank record AI052121 (10 July 1998).

The GenBank record provides an isolated nucleic acid encoding a polypeptide with biological activity, wherein said polynucleotide hybridizes to SEQ ID NO: 1 under stringent hybridization conditions. Nucleotides 9-574 of the nucleic acid taught in the GenBank record have 100% identity with the complement of nucleotides 1592-2157 of instant SEQ ID NO: 1. This nucleic acid would hybridize to SEQ ID NO: 1 under highly stringent hybridization conditions. Furthermore, the nucleic acid is considered to encode a polypeptide with biological activity because it would have the activity of being a substrate for a protease, for example, or it would be able to be used to raise antibodies, for example.

12. Claim 2 is rejected under 35 U.S.C. 102(a) as being anticipated by Ottolenghi et al. (Genomics, 64, 170-178; March 1, 2000).

Ottolenghi et al. teach an isolated nucleic acid encoding a polypeptide with biological activity, wherein said polynucleotide hybridizes to SEQ ID NO: 1 under stringent hybridization

conditions (nucleotide referred to therein as AF193873). The full nucleotide sequence of this nucleic acid is given in GenBank AF193873. Nucleotides 1-1760 of the nucleic acid taught by Ottolenghi et al. have 100% identity with nucleotides 386-2144 of instant SEQ ID NO: 1 (see alignment attached to the reference). This nucleic acid would hybridize to SEQ ID NO: 1 under highly stringent hybridization conditions. Furthermore, the nucleic acid is considered to encode a polypeptide with biological activity because it would have the activity of being a substrate for a protease, for example, or it would be able to be used to raise antibodies, for example.

Conclusion

13. Claims 1, 3-9, and 22-26 are free of the prior art. The prior art does not teach or suggest a nucleic acid comprising SEQ ID NO: 1 or having 99% sequence identity with SEQ ID NO: 1.

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1634

August 15, 2002

W. Gary Jones
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